Socioeconomic status and multimorbidity

A systematic review and meta-analysis

Pathirana, Thanya I.; Jackson, Caroline A.

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Socioeconomic status and multimorbidity: a systematic review and meta-analysis

Thanya I. Pathirana,[1] Caroline A. Jackson[2,3]

Abstract

Objectives: We performed a systematic review to identify, critically appraise and synthesise the existing literature on the association between SEP and multimorbidity occurrence.

Methods: We searched Medline and Embase from inception to December 2014. Where possible we performed meta-analysis to obtain summary odds ratios (ORs), exploring heterogeneity between studies through sub-group analysis.

Results: We identified 24 cross-sectional studies that largely reported on education, deprivation or income in relation to multimorbidity occurrence. Differences in analysis methods allowed pooling of results for education only. Low versus high education level was associated with a 64% increased odds of multimorbidity (summary OR: 1.64, 95% CI 1.41 to 1.91), with substantial heterogeneity between studies partly explained by method of multimorbidity ascertainment. Increasing deprivation was consistently associated with increasing risk of multimorbidity, whereas the evidence on income was mixed. Few studies reported on interaction with age or sex.

Conclusions: More methodologically robust studies that address these gaps and investigate alternate measures of social circumstances and environment may advance our understanding of how SEP affects multimorbidity risk.

Implications for public health: A deeper understanding of the socioeconomic and demographic patterning of multimorbidity will help identify sub-populations at greatest risk of becoming multimorbid.

Key words: chronic disease, multimorbidity, socioeconomic position, socioeconomic status, social class

The increasing prevalence of chronic conditions[1,2] and the growth of the ageing population has led to an increase in multimorbidity worldwide.[3] In this article, we distinguish between multimorbidity (the co-existence of two or more chronic conditions) and co-morbidity (co-occurrence of disease/s with a specific index disease). The impact of multimorbidity on the health and wellbeing of individuals, the burden on healthcare systems and the effect on economies has created a major global public health problem. A recent systematic review reported that the prevalence of multimorbidity among the general adult population in high-income countries ranges from 12.9% in participants aged 18 years and older to 95.1% in a community-dwelling elderly population aged 85 years.[4] However, while the prevalence of multimorbidity is highest among the oldest (above 85 years of age), the growing burden of multimorbidity among older adults still of working age and among lower socioeconomic groups in some countries is of particular public health concern.[5,6]

This expansion of morbidity is leading to individuals living longer but with more co-existing chronic disease from a younger age, placing an even greater burden on healthcare systems.

While multimorbidity incidence and prevalence is known to vary by measures of socioeconomic status (SEP), with an excess burden in lower socioeconomic groups, there are some gaps in our understanding of this relationship. It is unclear whether the association is true for all SEP measures and whether the magnitude of association varies by age, gender and country. Since different SEP variables measure different aspects of individual circumstances and environmental characteristics, a better understanding of which socioeconomic factors are more strongly associated with multimorbidity may help us to better understand the underlying mechanisms. In turn, this will help inform the design of intervention approaches aimed at preventing or reducing the development of multimorbidity.

Objectives

The objective of this review was to systematically identify, critically appraise and synthesise the existing literature on the association between SEP and multimorbidity occurrence.

Methods

This manuscript was prepared in accordance with the PRISMA guidelines.[7] The protocol for this review was not registered.

1. Centre for Research in Evidence based Practice, Faculty of Health Sciences and Medicine, Bond University, Queensland
2. Centre for Research Excellence in Women's Health in the 21st Century, Centre for Longitudinal and Life Course Epidemiology, School of Public Health, University of Queensland
3. Usher Institute for Population Health Sciences and Informatics, University of Edinburgh, UK
Correspondence to: Dr Thanya I. Pathirana, Centre for Research in Evidence based Practice, Faculty of Health Sciences and Medicine, Bond University, University Drive, Robina, QLD 4229; e-mail: thanya.pathirana@student.bond.edu.au
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Search strategy

We sought studies published in English in Medline and Embase between 1946 and 1974, respectively, and December 2014 reporting on the association between SEP and multimorbidity using a comprehensive electronic search strategy (Supplementary file 1: Appendix A) and perusal of reference lists of all relevant identified articles. We included terms for multimorbidity and comorbidity, since these are often used interchangeably. One author (TP) screened all references by title and abstract and, where necessary, the full text of the article. All potentially relevant articles were reviewed by the co-author, and any disagreements on inclusion were resolved through discussion between the two authors and consensus was reached.

Inclusion and exclusion criteria

We included studies of any quantitative design that reported on the occurrence of multimorbidity (defined by the co-occurrence of multiple conditions) with respect to any measure of SEP, in adult populations only. We excluded: qualitative studies; studies that included selected populations (e.g. patients with psychiatric conditions only, substance abuse problems or those who had undergone a specific medical procedure); and studies that reported on co-morbidity rather than multimorbidity. Where multiple articles on overlapping study populations were identified, we included the study with the largest population.

Data extraction

Both authors independently extracted information on: study design; study population; demographics; sample size; exclusion criteria; definition and ascertainment of multimorbidity; number of diseases ascertained; inclusion of mental health among chronic diseases; ascertainment and measure/s of SEP; and results, including numbers with and without multimorbidity, for the purpose of meta-analysis, where appropriate.

Data synthesis

We aimed to narratively summarise study findings or, where possible, combine study-specific estimates of effect using meta-analysis to obtain a pooled summary estimate. Due to the substantial variation in how SEP measures were defined, and/or the different methods of analysis used, meta-analysis was only possible for the association between education and multimorbidity. This SEP measure was the most consistently defined and a sufficient number of studies adopted the same statistical analysis approach (i.e. logistic regression) to allow us to formally pool the results.

Meta-analysis

We performed meta-analysis using Stata version 13 and adhered to the MOOSE guidelines.[8] We combined studies that either reported unadjusted odds ratios (ORs) with 95% confidence intervals (CIs) for the association between education and multimorbidity or presented raw numbers that allowed us to calculate ORs. Where we extracted raw numbers, we defined the non-multimorbidity comparison group as participants with fewer than two conditions, in line with the most common comparison group used across studies. Our rationale for pooling together minimally or unadjusted ORs was firstly to harmonise findings from studies, in order to facilitate inclusion of as many studies as possible. Studies varied in terms of: the type of effect estimates presented; whether they presented unadjusted and/or adjusted estimates; and specific factors adjusted for, and reference category used for effect estimates for education. Secondly, our interest lay in determining the association between SEP and multimorbidity without seeking to identify the mechanisms underlying the association. Extraction of only effect estimates adjusted for additional factors, some of which may lie on the causal pathway between SEP and multimorbidity, would therefore have potentially obscured the true nature of the association between SEP and multimorbidity. We obtained a pooled summary OR for the odds of multimorbidity comparing low versus high education using the Mantel Haenszel random effects model, assessing heterogeneity between studies using the chi^2 (Cochrane Q) and I^2 statistics. We sought to explore potential explanations for any observed heterogeneity using sub-group analysis. We aimed to assess the influence of three *a priori* determined study characteristics: age of study population; sex; and method of ascertainment of chronic disease (i.e. objective versus subjective, as described below). Where relevant studies on education and multimorbidity did not provide sufficient information to be included in the meta-analysis, we contacted the authors to obtain results in the necessary format. However, none of the authors who replied were able to provide this information, because they no longer had access to the datasets.

Results

We identified 2,496 articles, 63 of which were potentially relevant and underwent full-text review. Of 28 relevant studies, two were excluded[9,10] because the study populations overlapped with a third included study.[11] Two studies were excluded because they defined multimorbidity using a score that incorporated severity of disease (Figure 1).[12,13] The remaining 24 included studies were cross-sectional in design or entailed cross-sectional analysis of SEP factors related to multimorbidity (Table 1).[5,6,11,14-34] In general, participants were recruited through population-based primary care databases or national or regional surveys, with more than half (N=15) conducted in high-income countries. The number of chronic diseases included in each study ranged from 5 to 335 (Supplementary file 2: Appendix B), with just 12 studies reporting mental health diseases were included (Table 1).[5,6,11,14,19,20,23,24,28,29,31,33] Ten studies[5,11,22-25,28,29,31,33] ascertained multimorbidity through objective sources such as health records (which capture doctor-diagnosed conditions), while the remainder relied on self-report of doctor-diagnosed conditions by participants, which may be subject to recall error (Table 1). Multimorbidity was defined in 18 studies as the co-occurrence of two or more conditions, and in one study as the co-occurrence of three or more conditions, with the comparison group being fewer than two (or three) conditions (Table 1). The exceptions to this were the studies by Jerlui et al. and Marengoni et al. in which multimorbidity was compared to single morbidity.[21,24] In the remaining five studies, multimorbidity was analysed as a continuous count of conditions, without a cut-off being employed.

Most studies (N=17; 359,507 participants) measured SEP using education.[6,11,14-21,24,26,27,30-32,34] Eight studies (209,186 participants) reported on income[6,14,16,17,20,27,31,32] and six (2,332,316 participants) reported on deprivation.[5,23,25,28,29,34] In addition, one study reported on literacy,[22] three on occupational social class,[24,31,33] one on non-defined social class,[17] two on employment status[16,17] and one on self-perceived poverty.[21]

Table 1: Characteristics of identified studies.

Author, year	Country	Study population	Total N	Male (%)	Age (years)[a]	Definition of multimorbidity [comparison group]	Ascertainment of morbidities	Number of conditions included	Mental health included
Agborsangaya, 2012[14]	Canada	A representative sample of the adult (aged ≥18 years) population of the province of Alberta, as identified in the 2010 Patient Experience Survey by Health Quality Council of Alberta	5,010	47.7	46.7	≥2 concurrent conditions [<2 conditions]	Self-report via telephone-administered survey questionnaire	16	Y
Ahluwalia, 2005[15]	US	Non-institutionalised, non-pregnant women aged 18-44 years, identified from the Behavioural Risk Factor Surveillance System, an ongoing random digit dialled telephone survey of 50 States;	163,566	0	Mean NR Range 18-44	≥2 concurrent conditions [no formal statistical comparison made]	Self-report via telephone-administered survey questionnaire	5	N
Alaba, 2013[16]	South Africa	Stratified two-stage cluster sampling of 53 district councils of South Africa, including adults aged ≥15 years; for this study adults aged ≥18 were included	11,638	39	40	≥2 concurrent conditions [<2 conditions]	Self-report of doctor-diagnosed condition	6	N
Andrade, 2010[17]	Brazil	Non-institutionalised adults aged ≥18 years included in a household survey of two boroughs of Sao Paulo	1,464	57.4	Mean NR (82% aged <60)	Morbidity included in modelling as a continuous variable	Face-to-face interviews, with information on morbidities obtained via self-reported doctor diagnosis of various conditions	8	N[b]
Barnett, 2012[5]	Scotland	Patients of any age registered with one of 314 GP practices, covering one third of the Scottish population	1,751,841	49.5	Mean NR (83% aged <65)	≥2 concurrent conditions [<2 conditions]	GP medical records and prescription data	40	Y
Droomers, 2004[18]	Netherlands	Respondents aged 25 or over included in the Netherlands Health Interview Surveys from 1990-1998 which included non-institutionalised persons	53,339	NR	Mean NR (all ≥25)	≥2 concurrent conditions [<2 conditions]	Self-report in questionnaire	14	N
Enroth, 2013[19]	Finland	Survey of adults aged 90+ living in Tampere, irrespective of dwelling place (80% of eligible population responded)	1,283	19	Mean NR (All ≥90)	≥2 concurrent conditions [<2 conditions]	Self-report of doctor-diagnosed conditions	6	Y
Hosseinpoor, 2012[20]	41 low and middle-income countries	Data from the 2002-04 World Health Survey of adults aged ≥18 years in 41 low and middle-income countries; surveys are nationally representative except in 6 countries where WHS is conducted in geographically limited regions	170,298	45.5	Mean NR (all >18)	≥2 concurrent conditions [<2 conditions]	Self-report in questionnaire; symptom-based classification based on symptoms in previous 12 months used for all conditions except diabetes, which was reported directly; diabetes by self-report	5	Y
Hudon, 2012[13]	Canada	Regular patients aged ≥18 years attending a family medicine clinic (primary care) of a regional health center in Saguenay, Quebec	103	35	49.9	Used a multimorbidity score	Self-reported questionnaire using simplified version of the Disease Burden Morbidity Assessment, including 11 of 21 diseases included in the original instrument, based on the high prevalence of these diseases in this setting	11	N
Jerliu, 2013[21]	Kosovo	A nationwide, population-based representative sample of adults aged ≥65 years	1,890	50.2	73.4	≥2 concurrent conditions [1 condition]	Self-report via an interviewer-administered questionnaire	Unclear*	Unclear*
Khanam, 2011[22]	Bangladesh	Randomly selected individuals age >=60 from two areas of a rural area of Bangladesh, based on the sampling frame of the Health and Demographic Surveillance System	452	45.1	69.5	≥2 concurrent conditions [<2 conditions]	Clinical examination by physicians, with independent evaluation by senior physicians/geriatricians	9	N
Macleod, 2004[23]	Scotland	Patients aged 18 or over registered at one practice in an area of high deprivation in Glasgow City	7,286	NR	Mean NR (76.7% aged <65)	≥2 concurrent conditions [<2 conditions]	GP records	16	Y
Marengoni, 2008[24]	Sweden	Participants in the first follow up of the Kungsholmen Project, a study on elderly people (aged ≥75 years in October 1987) living in Stockholm.	1,099?	NR	84.6	≥2 concurrent conditions [1 condition]	Clinical assessment by a physician, medical history (from Stockholm inpatient register that records discharge diagnoses from Stockholm hospitals), laboratory data and current drug use.	30	Y
Mercer, 2007[25]	Scotland	Consecutive unselected patients of one GP nominated from medium-sized practices in the upper or lower quartiles of deprivation in 4 healthboard regions in West of Scotland; 26 GPs included	3,044	NR	44.6**	Morbidity assessed as a count, not a cut-off	GP records	NR, but based on GP records so presumably all conditions included	NR

Table 1 continued: Characteristics of identified studies.

Author, year	Country	Study population	Total N	Male (%)	Age (years)[a]	Definition of multimorbidity [comparison group]	Ascertainment of morbidities	Number of conditions included	Mental health included
Nagel, 2008[26]	Germany	Heidelberg cohort of European Prospective Investigation in to Cancer and nutrition (EPIC) recruited from general population. Cross-sectional analysis of multimorbidity using data on prevalent chronic conditions collected at baseline and during follow-up	13,781	52.9	Median 55-58 across male and female subgroups	≥2 concurrent conditions [<2 conditions]	Prevalent diseases identified at recruitment by face to face interviews; new diseases identified by active follow up through questionnaire on physician diagnosed chronic conditions. Cancer cases verified with medical records and validation studies conducted for incident cases of diabetes, MI, asthma and stroke	24	N
Neeleman, 2001[27]	Netherlands	Participants of the 1996 wave of NEMESIS, a study of the incidence and prevalence of mental disorders in the general population; random sampling of 90 municipalities of adults aged 18-64 years	7,076	NR	NR	Morbidity assessed as a count, not a cut-off	Self-report based on interviewer-administered questionnaire	30	N[b]
Orueta, 2013[28]	Spain	Adults aged ≥65 years covered by public health insurance in the Basque country on 31st August 2011 for at least 6 months in the previous year, regardless of whether or not they had made any contact with or use of Basque Health Service	452,698	42.5	Mean NR	≥2 concurrent conditions [<2 conditions]	Primary care electronic medical records, hospital admissions, outpatient care databases and prescription data	47	Y
Salisbury, 2011[29]	England	Random sample of patients aged 18 or over registered with one of 18 General Practitioners on index date of 1 April 2005	99,997	NR	NR	≥2 concurrent conditions [<2 conditions]	GP records	19	Y
Santos Machado, 2013[30]	Brazil	Simple random sampling of women aged ≥50 living in 68 census districts of the city of Campinos, Sao Paulo	622	0	Mean NR (61.3% aged >60)	≥2 concurrent conditions [<2 conditions]	Self-report based on interviewer-administered questionnaire	12	N
Schafer, 2012[31]	Germany	Patients born between 1st July 1923 and 30th June 1943 who consulted GP at one of 158 General Practices in 8 study centres were randomly selected	3,189	59.3	74.4	Morbidity included in modelling as a continuous variable	GP interviews using standardized instrument covering 46 chronic conditions	46	Y
Taylor, 2010[6]	Australia	Participants aged ≥18 years from the North West Adelaide Study, a population-based cohort study; included those from stage 2 of the cohort study, which involved all or a combination of: a computer assisted phone interview; self-complete questionnaire; and a biomedical examination at a clinic	3,206	NR	Mean NR (75% aged <60)	≥2 concurrent conditions [<2 conditions]	Self-report of doctor diagnosed condition	7	Y
Tucker-Seeley, 2011[32]	US	Respondents aged ≥50 years from 2004 wave of the Health and Retirement study	7,305	46.4	65	≥2 concurrent conditions (for this review) [<2 conditions]	Self-report of doctor diagnosed condition	6	N
Uijen, 2008[33]	Netherlands	Patients of all ages enlisted in the Continuous Morbidity Registration, Nijmegen, which includes 4 General Practices, including 10 GPs with approximately 13,500 enlisted patients;	13,584	NR	Mean NR Range 0 - >75	Examined distribution of 0,1,2,3 and ≥4 conditions by SEP	GP records	NR[c]	Y
Van den Akker, 1998[11]	Netherlands	Participants identified from Registration Network Family Practices, a continuous computerised primary care database including 42 GPs in 15 different practices	60,857	48.7	Mean NR (80% aged <60)	≥2 concurrent conditions [<2 conditions]	GP records	335	Y
Walker, 2007[34]	Australia	Participants aged ≥ 20 years in the Australian 2001 National Health Survey or the 2003 Survey of Disability Ageing and Carers, both of which are nationally representative	17,450	45	Mean NR	≥3 concurrent conditions [<3 conditions]	Self-report in household surveys	NR	NR

** Survey included questions on which groups of diseases participants had and also included an open-ended question on other chronic conditions*

*** Weighted mean calculated from data presented in paper*

a: Mean unless specified otherwise

b: Psychiatric conditions analysed separately

c: Total number of conditions not reported, but included all obligatory and conditionally registered chronic diseases recorded in the Continuous Morbidity Registration

NR = not reported; GP = general practitioner; MI = myocardial infarction; SEP = socioeconomic position

Education

Six studies used comparable methods of analysis and reported ORs with 95% CI for the association between education and multimorbidity. An additional 4 studies[16,30,32,34] reported sufficient raw numbers to allow the calculation of unadjusted ORs. Thus 10 studies presenting information on 13 study populations (N=122,858 participants) were included in the meta-analysis. There was substantial heterogeneity between studies (I^2=89.3%; p-value<0.001), therefore we must be cautious when interpreting the pooled effect estimate. For what it's worth, low education was associated with a 64% increased odds of multimorbidity (summary OR: 1.64, 95%CI 1.41 to 1.91; Figure 2). ORs were adjusted for age in only three[11,21,24] of the 12 study populations. However, age-adjusted odds ratios were consistent with the overall finding, with low education associated with a 60% increased odds of multimorbidity.[21,24] Sub-group analyses suggested that the effect of low education on multimorbidity varied according to the method of disease ascertainment, with the effect stronger among studies relying on self-report of chronic conditions than in studies using healthcare records to ascertain disease history (summary ORs 1.79, 95%CI 1.45 to 2.21 and 1.40, 95%CI 1.28 to 1.53, respectively; Figure 2). Unfortunately, the majority of studies reported findings for both genders combined, limiting scope for investigation of consistency across men and women. When we grouped studies according to age (using a cut-off of 65 years, which was the most common age restriction applied across studies), the association appeared stronger in older than younger populations (Supplementary Table 1). However, very few studies actually investigated age and sex within the same study population.[6,14,19,26] Eleven study populations among six studies reported odds ratios adjusted for other sociodemographic factors and (less commonly) lifestyle behaviours.[6,11,14,16,21,26] The pooled summary estimate indicated an attenuation of the association between education level and multimorbidity (pooled summary OR 1.27, 95%CI 1.21 to 1.33; Supplementary Figure 1), with no heterogeneity between studies (I^2=0%; p-value=0.52). A funnel plot for the association between education and multimorbidity revealed no suggestion of publication bias (p-value for small study effects=0.95; Figure 3).

Seven studies (N=236,649 participants) reporting on education were not included in the meta-analysis due to: incomparable methods of analysis and insufficient data to calculate ORs;[17,19,20,27,31] lack of CIs for effect estimates;[18] and insufficient data to calculate ORs.[15] Findings from almost all of these studies were consistent with those included in the meta-analysis.

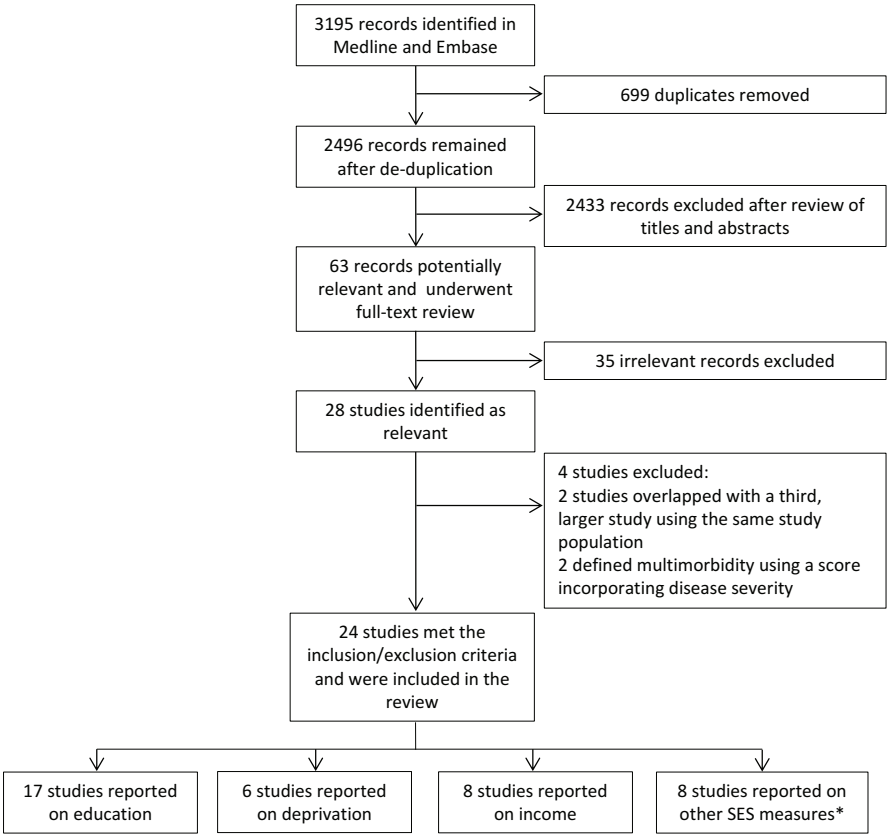
Deprivation

The association between deprivation and multimorbidity was generally investigated using primary care datasets. As such, analyses were unadjusted for health behaviours, apart from one study that used survey data.[34] In all studies, higher deprivation level was associated with a statistically significant greater risk of multimorbidity (Table 2). Differing methods of analysis and data presentation precluded formal pooling of these studies. Just two studies stratified by age and/or gender. In one study, the association between deprivation and multimorbidity was most striking in those aged 40–70 years, with the gap narrowing in those aged over 70 years. Young and middle-aged adults living in the most deprived areas had rates of multimorbidity equivalent to those aged 10–15 years older in the most affluent areas.[5] Orueta et al. stratified by both age and sex.[28] The study population was aged 65 years or over and so, in contrast to the latter study, there was a less obvious narrowing of the deprivation gap in multimorbidity risk by age. Disparities were, however, larger in women compared to men.

Income

The findings for income in relation to multimorbidity risk were inconsistent across studies (Table 2). Four studies reported an increasing risk of multimorbidity with decreasing income,[13,14,20,31] three of which had adjusted for demographic factors and education level.[13,14,20] In contrast to their findings on education and multimorbidity, the South African study reported that multimorbidity risk *increased* with increasing income. This suggests that some SEP measures, such as income, might actually be positively associated with risk of chronic disease and multimorbidity in some low-income countries.[16] A Brazilian study reported no significant association between income and multimorbidity,[17] while a US study reported an association between income and multimorbidity in unadjusted analyses

Figure 1: Flow diagram of literature search and included studies.



only.[32] An Australian study found the risk of multimorbidity increased with decreasing income level among those aged 45–59 years, but not 60 years or over,[6] whereas no age differences were observed in a Canadian study.[14] Just one study reported findings stratified by sex,[20] with low income associated with increased risk of multimorbidity in men in both low- and middle-income countries, but no association observed in women in low-income countries after adjusting for education, marital status and rural/urban area.

Other SEP measures

Evidence for the association between other SEP measures and multimorbidity is limited. Occupational social class was associated with multimorbidity in one study[33] (although statistical significance was not tested), but not in two other studies.[24,31] Social class (not defined) was not

Figure 3: Funnel plot for the association between education and multimorbidity.

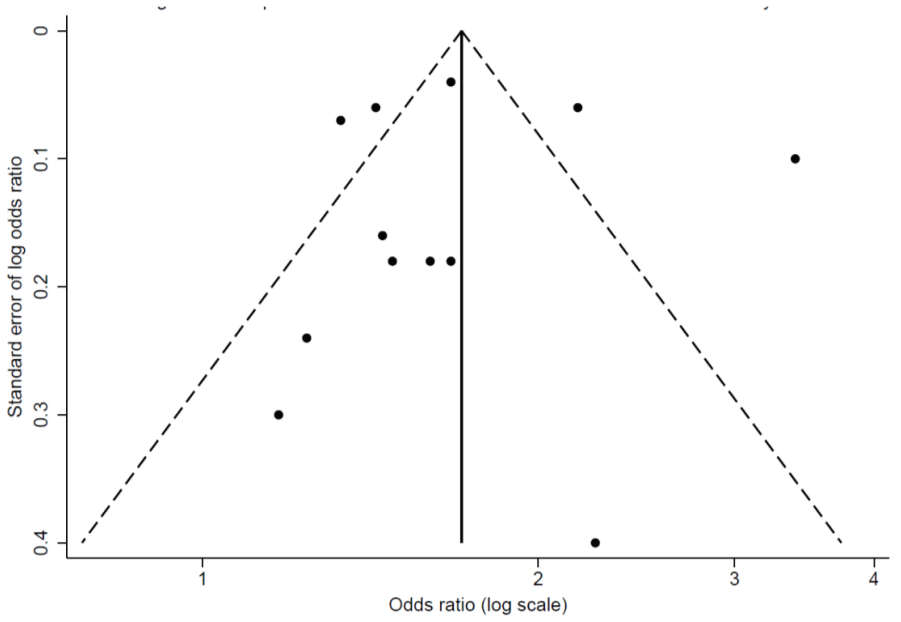
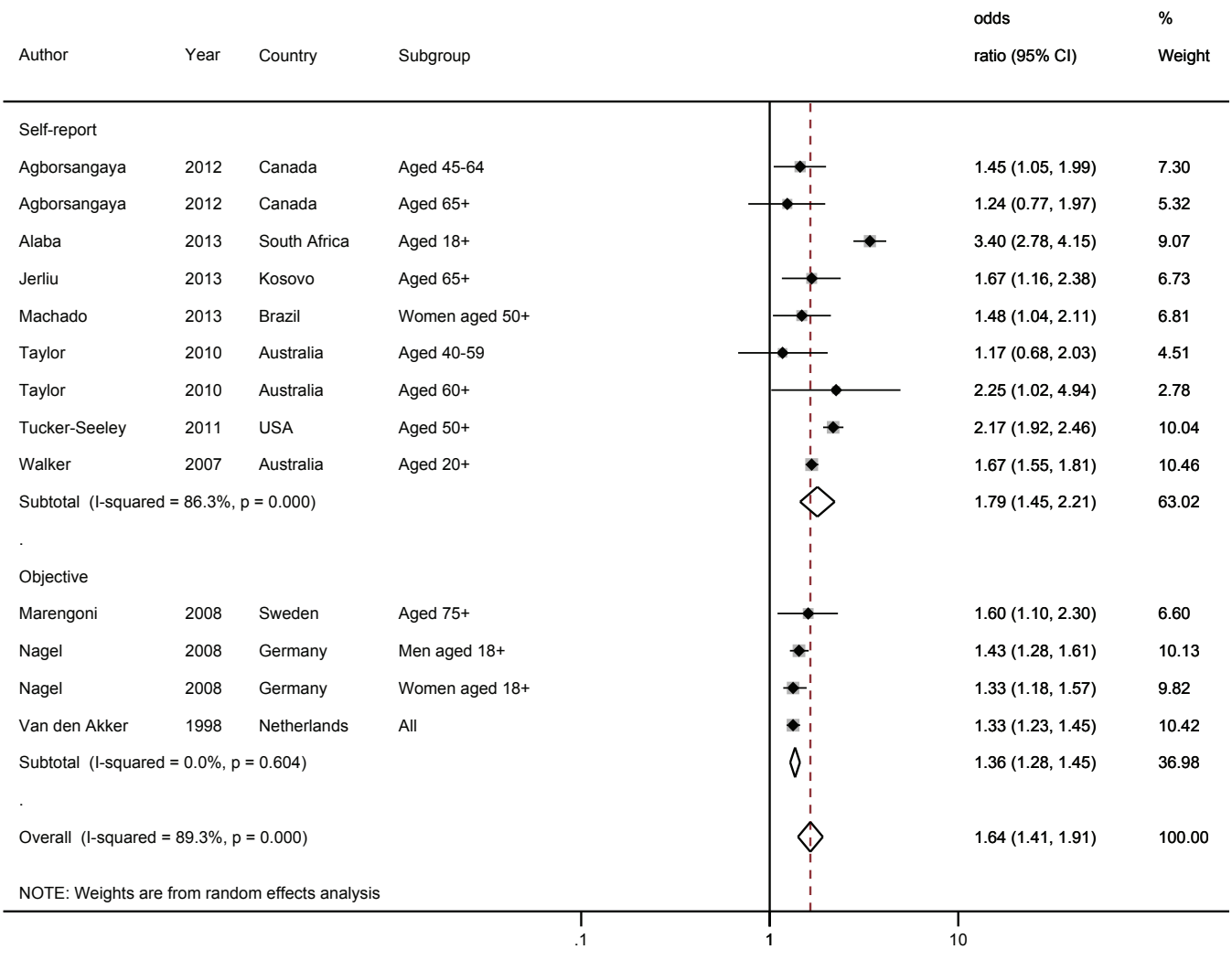


Figure 2: Meta-analysis of the association between education and multimorbidity, showing study-specific and summary odds ratios with 95% confidence intervals, and sub-group analysis according to whether multimorbidity was ascertained using objective or subjective methods.



associated with multimorbidity in a Brazilian study.[17] Employment status was associated with a decreased risk of multimorbidity in one study[16] but not in another.[17] A study in Bangladesh found an association between low literacy level and increased multimorbidity risk, which did not persist after adjustment for other factors.[22] Finally, one study reported that self-perceived poverty was associated with increased multimorbidity risk.[21]

Discussion

We identified a high number of studies examining the occurrence of multimorbidity according to SEP, primarily in high-income settings. Education was most commonly studied, with meta-analysis showing that low- versus high-education level was significantly associated with an increased odds of multimorbidity, albeit with substantial heterogeneity between studies. Higher area-based deprivation was consistently associated with greater multimorbidity, but the picture was less clear for income. There is little evidence on how the associations between SEP and multimorbidity varies by sex and age.

The association between each of education and deprivation and prevalence of multimorbidity is unsurprising, given the well-established evidence base for the association between these SEP measures and the risk of various individual chronic diseases.[35-37] The less consistent association between income and multimorbidity may reflect differences in setting and population and the fact that income is less of a robust SEP measure particularly among retired people. Few studies stratified associations between SEP and multimorbidity by age and/or sex, with conflicting results from the studies that did stratify. Findings from one of the largest studies indicated that multimorbidity onset may occur at a younger age in the most deprived versus affluent areas.[5] While further studies are needed to fully understand the reasons for this disparity, these findings have implications for intervention approaches aimed at reducing multimorbidity,[38] which need to be targeted at much younger age groups, particularly among those living in adverse circumstances.

While the underlying reasons for the observed association between education, deprivation and risk of multimorbidity are likely complex and multifactorial, intermediary factors such as lifestyle, access to and use of health services, and neighbourhood context will be important.[39] Studies on deprivation and multimorbidity did not tend to adjust for any of these factors, while the few studies on education and multimorbidity that did adjust for lifestyle behaviours found that the association persisted. Developing constructs that capture more refined elements of socioeconomic circumstances, including for example social capital, might also yield a richer understanding of why inequalities in multimorbidity exist.[40] Fresh perspective on this may come from the field of syndemics, which refers to the synergistic clustering of health conditions that results from and contributes to complex social and economic inequalities. This theory highlights the importance of the wider context of multimorbidity and reinforces the importance of understanding how macro- level factors interact with and promote the clustering of chronic diseases at the population level.[41] We found relatively little data on SEP and multimorbidity occurrence in low- and middle-income countries.[16,17,20-22,30] While some measures of SEP may actually be associated with an increased risk of various chronic conditions in some low-income

Table 2: Summary of findings from studies on the association between each of area-based deprivation/ disadvantage and income, and multimorbidity.

Study, year	Country	Measure of deprivation/income	Effect on multimorbidity*
Area-based deprivation[a]			
Barnett, 2012[5]	Scotland	Carstairs Deprivation Index; based on census information for postcode sectors	↑
Macleod, 2004[23]	Scotland	Carstairs Deprivation Index; based on census information for postcode sectors	↑
Mercer, 2007[25]	Scotland	Multiple index of deprivation score based on geographical areas	↑
Orueta, 2013[28]	Spain	Geographical deprivation index based on census information for small geographical units	↑
Salisbury, 2011[29]	England	Townsend Deprivation Index; based on census information for postcode sectors	↑
Walker, 2007[34]	Australia	Socioeconomic indexes for Areas (SEIFA) Index of relative disadvantage; based on census information for geographical areas	↑
Income[a]			
Agborsangaya, 2012[14]	Canada	Annual household income; 4 categories ranging from <$30,000 to ≥$100,000	↑[b]
Alaba, 2013[16]	South Africa	Quintiles of annual household income	↓[c]
Andrade, 2010[17]	Brazil	Family income; categorised into top 25%, middle 50% and lowest 24%	↔
Hosseinpoor, 2012[20]	Low- and middle-income countries	An index of the long-running economic status of households based on owning selected assets and/or using certain services was created to give a household wealth index, split into quintiles	↑[b]
Hudon, 2012[13]	Canada	Annual household income; 4 categories ranging from <$10,000 to ≥$50,000	↑[b]
Neeleman, 2001[27]	Netherlands	Annual income; 3 categories – lowest to highest	↑ (unadjusted) ↔ (adjusted[b])
Schafer, 2012[31]	Germany	Household-size adjusted net income per month	↑ (unadjusted)
Taylor, 2010[6]	Australia	Annual household income; 3 categories; ranging from <$20,000 to >$80,001	↑ for ages 45-59 (unadjusted) ↔ for ages 45-59 (adjusted[d]) ↔ for ages ≥60
Tucker-Seeley, 2011[32]	US	Lifetime earnings, based on average annual lifetime earnings during young and middle adulthood	↑ (unadjusted) ↔ (adjusted[b])

*↑ = increasing deprivation is statistically significantly associated with an increased risk of multimorbidity and decreasing income is statistically significantly associated with an increased risk of multimorbidity; ↓ = decreasing income is associated with a decreased risk of multimorbidity; ↔ = no statistically significant association between income and multimorbidity

a: For deprivation, all results are unadjusted for other factors; for income, unless specified, arrows represent the results for both unadjusted and adjusted analyses;

b: Adjusted for demographic factors and education

c: Adjusted for sociodemographic factors, smoking, obesity, health facility visits and civic participation

d: Adjusted for demographic, risk factor and health-related variables (health service use and medicines)

settings, once these countries undergo epidemiological transition we can expect to see greater burden of multimorbidity among lower socioeconomic groups.

Methodological shortcomings of some of the identified studies limit the robustness of the results. In particular, given the cross-sectional nature of the existing studies on this topic, we must exert caution when drawing conclusions about SEP and the association with multimorbidity incidence. Education is perhaps an exception, given that it is a marker of young adult socioeconomic status. However, ability to work, nature of occupation, level of income and to some extent area-based deprivation could themselves be influenced by a person's level of morbidity. The quality of the evidence from existing studies is mixed, with aspects of the study design in many instances potentially introducing bias and contributing to significant heterogeneity between studies. Specifically, some studies included a limited number of morbidities, which may have underestimated the prevalence of multimorbidity and affected the association with SEP in an unpredictable manner.[15,16,19,20,32] Some studies ascertained disease occurrence through self-report,[6,14,16,21,30,32,34] which we demonstrated in sub-group analyses to lead to an overestimation of the association between education and multimorbidity.

Not all studies included mental health conditions in their definition of multimorbidity, and so conclusions on the association between SEP and multimorbidity in these studies relate specifically to physical disease multimorbidity. There were no differences in study findings between those that did include mental disorders versus those that didn't. Mental health disorders are likely to be under-ascertained, particularly in low- and middle-income settings where substantial treatment gaps for mental health exist.[42] However, studies on multimorbidity should endeavour to capture both physical and mental health disease occurrence, which are known to be strongly linked.[43]

Finally, although multimorbidity was consistently defined as two or more conditions in the majority of identified studies, there is no universally accepted definition of multimorbidity.[44] A simple count of conditions may be too crude and may not necessarily reflect 'burden' of disease in terms of morbidity that impacts on quality of life for example. Different conditions or combinations of conditions may also relate to SEP to differing degrees, associations that would be masked by the use of a single multimorbidity construct. In some scenarios, co-morbidity or frailty measures might be more applicable or appropriate than a measure of multimorbidity. Also, there is no consensus as to what constitutes a single disease when studying multimorbidity. There is some support for a definition of multimorbidity that reflects the existence of disease in multiple body systems as opposed to a count of conditions, irrespective of whether they reflect the same 'bodily' disease.[45]

To our knowledge, this is the first systematic review of studies investigating the association between SEP and multimorbidity. Our review identifies important methodological issues of studies on multimorbidity, which have implications for future primary studies. Our review also identifies important gaps in our understanding of how SEP relates to multimorbidity, which should inform the design of future research.

Our review does have some limitations. As discussed above, some of these relate to the limitations of the studies themselves. Although we could not include all identified studies on education in our meta-analysis, it is reassuring that the findings from studies not included were in keeping with the meta-analysis findings. However, we were unable to identify all underlying explanations for the observed heterogeneity. Due to limited resources, we did not search grey literature or include non-English published articles. Finally, while we did carefully consider and critique the methodological quality of included studies, we did not formally assess methodological quality using a quality assessment tool.

Conclusions

Existing evidence demonstrates that low education level and living in a deprived area are associated with an increased risk of multimorbidity. Much of this evidence stems from studies based in high-income settings, some of which are limited by methodological shortcomings. Future studies should: minimise the risk of reverse causation through prospective study of the temporal association between socioeconomic factors and multimorbidity risk; and use objective ascertainment of a comprehensive list of chronic conditions, including mental health conditions. More broadly, further investigation into how multimorbidity should be defined is needed, with a view to obtaining a universally accepted definition or suite of definitions that can be used for research. There is an urgent need for more studies in low- and middle-income countries, where multimorbidity is already a significant public health challenge. A deeper understanding of the mechanisms underlying these associations should help to identify pathways amenable to intervention aimed at reducing multimorbidity in the most vulnerable groups.

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Supporting Information

Additional supporting information may be found in the online version of this article:

Supplementary File 1: Appendix A Search Strategy in Medline.

Supplementary File 2: Appendix B Details of chronic conditions included in the definition of multimorbidity in each study.

Supplementary Table 1: Summary of sub-group meta-analyses for the association between education and multimorbidity.

Supplementary Figure 1: Meta-analysis of the association between education and multimorbidity, among studies which reported adjusted study-specific and summary odds ratios, with 95% confidence intervals .